Results and risk factors of high lactate level after open-heart surgery

The results of high lactate level in open heart surgery

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Abstract

Aim: The aim of this study is to determine risk factors associated with hyperlactatemia developing after open-heart surgery and to investigate the effects of hyperlactatemia on mortality and morbidity.

Material and Methods: Five hundred seventeen adult patients who underwent elective open-heart surgery were enrolled prospectively. Lactate values were recorded before induction and at the 2nd, 6th, 12th, and 24th hours of admission in the intensive care unit. Lactate cut-off value was found to be 3.05 mmol/L (sensitivity 86.7% and specificity 87.6%) with ROC analysis (AUC =, 911; p <0.01); Group 1 (Lactate <3.05 mmol/L, n = 442) and Group 2 (Lactate ≥ 3.05 mmol/L, n = 75).

Results: Patients with HL had significantly higher EuroSCORE II value (p = 0.018), longer CPB (p = 0.000), and ACCtimes (p = 0.000), and more on-pump need for inotropic agents (p = 0.000). In the HL group, the ventilation time was 25.0 ± 26.9 hours, the length of stay in ICU was 5.4 ± 4.3 days, and the length of hospital stay was 10.9 ± 6.0 days (p <0.01). The mortality rate was 17.3% (p =. 000). In multivariate analysis, CPB time, use of inotropic agents in the intensive care unit, use of IABP and ECMO, and prolonged ventilation time (> 24h) were found to be independent risk factors for hyperlactatemia (p <0.05).

Discussion: According to our study, the lactate threshold at the 24th hour of 3.05 mmol/L predicted postoperative mortality in adult patients who underwent open-heart surgery.

Keywords

Cardiac Surgery, Hyperlactatemia, Morbidity, Mortality, Risk factors

Introduction

Hyperlactatemia (HL) is a common clinical condition following open-heart surgery and has been reported to be associated with morbidity and mortality [1-6]. It has been stated in the literature that high lactate levels result in many complications, including mortality, in the postoperative period [7-10].

Although the exact mechanism of HL in patients undergoing open-heart surgery is not fully explained, many factors are known to play a role in this issue [7]. Some of the causes of postoperative lactate elevation include comorbidities, organ perfusion during the cardiopulmonary bypass period, and difficulties in intraoperative anesthesia management. In addition, decreased cardiac performance and decreased oxygen supply to tissues in the postoperative period have been stated to be the most important cause of postoperative hyperlactatemia [1-7, 11, 12].

In open-heart surgery, it is important whether hyperlactatemia, which occurs as a result of different mechanisms, predicts complications in the post-operative period or to what extent it determines [2,7].

Since there is no perioperative clinical follow-up data in classifications such as EuroSCORE for risk determination before open-heart surgery [7,13]. Therefore, it should be known at what intervals and for how long lactate levels should be monitored to foresee the mortality and morbidity that may develop in the postoperative period. Thanks to the determined risk factors, perioperative anesthesia management, and intensive care follow-up can be made more efficiently and hospital stay periods can be shortened.

In this study, we aimed to investigate how lactate levels affect morbidity and mortality in the first 24 hours postoperatively in patients who underwent open-heart surgery, as well as the factors associated with hyperlactatemia in patients.

Material and Methods

This prospectively planned study was conducted in 517 patients who underwent elective open-heart surgery in our clinic between January 2019 and October 2019, after obtaining Ethics committee approval (Decision number: 2018/6/68, Date 15.11.2018).Those who underwent off-pump surgery, those who had a total circulatory arrest, redo cases, emergency cases, those who had congenital heart surgery, those who underwent heart transplantation and received left ventricular assist device, those who died intra operatively, and those under the age of 18 were excluded from the study.

Our cardiac anesthesia protocol was applied to all patients who provided informed consent before surgery. For the induction of anesthesia, 3mg.kg-1propofol, 0.6 mg.kg-1 rocuronium, and 2-3μgr.kg-1 fentanyl were administered. Maintenance of anesthesia was provided by inhalation of sevoflurane (MAC 1-2%) with 70% O2+ 30% air, and intermittent midazolam, fentanyl, and rocuronium during cardiopulmonary bypass (CPB). Invasive arterial pressure, central venous pressure, peripheral oxygen saturation, 12-lead ECG, and nasal temperature monitoring were performed in all patients.

Operations were performed in company with cardiac arrest using moderate hypothermic (28-320C), antegrade, and/or retrograde cold blood cardioplegia with cardiopulmonary bypass following standard sternotomy and heparinization. During CPB, non-pulsatile flow was maintained between 2.2-2.6 L/min/m2, the mean CBP pressure 60-70 mmHg, Hct> 22%, and blood glucose between 100-180 mg/dL. For the targeted mean CPB perfusion pressure, the perfusion flow was increased and/or vasopressor was used when required. CPB output was returned to ACT basal value with protamine.

Blood lactate levels were measured at fixed time intervals. Lactate values from the arterial blood sample were obtained from the standard arterial blood gas analyzer (ABL 800flex, Akın medical). The initial sample (basal) was collected immediately after the intra-arterial catheter was inserted. Subsequent samples were collected at the following intervals: 2nd, 6th, 12th, and 24th hours after admission to the intensive care unit. Mean arterial pressure (MAP) was measured and recorded before the induction of anesthesia. Mean CPB pressure and mean CPB flow were measured and recorded every 20 minutes during the pump.

Data collection

Preoperative data, gender, age, BMI, comorbidities (diabetes, hypertension, dyslipidemia, chronic obstructive pulmonary disease, chronic renal failure, cerebrovascular event (CVD), carotid disease, past MI), EuroSCORE II classification, MAP, serum creatinine and ejection fraction (EF), and type of surgery of each patient were recorded. As intraoperative data, CBP time, aortic cross-clamp (ACC) time, lowest on-pump hematocrit value, mean CBP pressure, the difference between MAP and mean CPB pressure, mean CPB flow, on-pump inotropic agent requirement, and on-pump use of erythrocyte suspension were recorded. As postoperative data, mechanical ventilation time, intensive care unit (ICU) stay and hospital stay, complications (infection, CVD, surgical bleeding, reoperation, dialysis, prolonged mechanical ventilation (> 24 h), use of inotropic agents, IABP, ECMO use), and mortality were recorded.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS 22.0 program. Results were expressed as number of patients and percentage values for categorical variables and as mean ± standard error for continuous variables.

ROC analysis was performed for lactate values at the 2nd, 6th, 12th, and 24th hours of ICU, which best describe the mortality status, and the cut-off value was determined.

In the comparison of the two groups, Chi-square and Fisher's exact tests were used for qualitative variables, and Independent Sample t-test and Mann Whitney U tests for quantitative variables. Univariate and multivariate logistic regression analyses were used to determine risk factors associated with HL. A p-value of <0.05 was considered statistically significant.

Results

Open-heart surgery was performed on 517 patients (115 Females, 402 Males, age range; 30-82 years) at Koşuyolu Heart Hospital between January 2019 and October 2019. Figure 1 shows the ROC curve comparing the state of predicting mortality of lactate levels at the 2nd, 6th, 12th, and 24th hours of postoperative ICU. In the ROC analysis, among the lactate values measured at the 2nd, 6th, 12th, and 24th hours of the ICU, the cut-off value for lactate at the 24th hour (AUC =, 911;

Table 1. Preoperative Baseline Characteristics

	Lactate<3,05 mmol/L n=442	Lactate ≥3,05 mmol/L n=75	p
Famele	113 25,6%	22 29,3%	0,492
Male	329 74,4%	53 70,7%	
Age (years)	61,7±10,1	63,5±12,1	0,169
BMI (kg/m2)	28,5±4,4	28,4±5,1	0,778
EuoroSCORE II	1,5±1,2	1,9±1,5	,018*
MAP (mmHg)	100,5±16,2	97,3±16,3	0,114
HT	199 45,0%	29 38,7%	0,305
DM	193 43,7%	26 34,7%	0,145
COPD	49 11,1%	10 13,3%	0,571
Cerebrovascular event	31 7,0%	70 93,3%	0,589
Chronic renal failure	12 2,7%	5 6,7%	0,076
Carotid artery stenosis	126 28,5%	26 34,7%	0,279
Previous myocardial infaction	84 19,0%	17 22,7%	0,46
Dyslipidemia	56 12,7%	6 8,0%	0,25
Serum creatinine (μmol/L)	1,0±,5	1,1±,9	0,079
Lactate (mmol/L)	1,80±89	1,94±,81	0,213
LVEF (%)	57,6±9,6	58,4±9,8	0,51
LVEF<45%	39 8,8%	8 10,7%	0,608
Type of operation			
Single valve surgery	55	14	
Complex valve surgery	32	6	
CABG	327	43	
CABG and valve surgery	28	12	

NOTE: Data are presented as n or frequenecy (%) or mean±SD. **p<0,01 *p<0,05, BMI: Body Mass Index, MAP: Mean arterial pressure, HT: Hypertension, COPD: Chronic obstructiv epulmonary disease, DM: Diabetes Mellitus, CABG: Coronary artery bypass grafting, LVEF: Left ventricular ejection fraction

Table 2. Peroperative characteristics and Mortality

	Lactate<3,05 mmol/L n=442	Lactate≥3,05 mmol/L n=75	P
CPB duration (min)	124,0±38,7	162,4±54,2	,000**
ACC time (min)	79,8±35,0	107,1±48,1	,000**
Nadir hematocrit on CPB (%)	25,0±3,9	24,6±4,6	0,415
Transfusion during CPB with RBCs	98 22,2%	21 28,0%	0,268
Mean CPB pressure (mmHg)	74,8±8,9	74,0±7,3	0,462
MAP- mean CPB pressure (mmHg)	25,9±14,9	24,0±16,1	0,333
Mean CPB flow (L/min)	4,2±,4	4,2±,5	0,808
Need of inotropic agents on CPB	186 42,1%	52 69,3%	,000**
Ventilation time (hours)	11,1±8,5	25,0±26,9	,000**
Prolongedventilation (>24 h.)	18 4,1%	23 30,7%	,000**
Infections	17 3,8%	2 2,7%	0,616
Bleeding	36 8,1%	8 10,7%	0,469
Re-operation	23 5,2%	11 14,9%	,002**
Cerebrovascular event	8 1,8%	4 5,3%	0,061
Dialysis	14 3,2%	8 10,7%	,003**
IABP	6 1,4%	15 20,0%	,000**
ECMO	1 0,2%	7 9,3%	,000**
Use of inotropic agents in ICU	107 24,2%	45 60,0%	,000**
ICU staying period (days)	2,8±2,0	5,4±4,3	,000**
Hospitalization period (days)	7,5±3,3	10,9±6,0	,000**
Mortality	2 0,5%	13 17,3%	,000**

NOTE: Data are presented as n or frequenecy (%) or mean±SD. **p<0,01 *p<0,05, CPB: Cardiopulmonary bypass, ACC: Aortic cross-clamp, MAP: Mean arterial pressure, IABP: Intra-aortic balloon pump, ECMO: Extracorporeal Membrane Oxygenation

Table 3. Logistic Regression Analysis for Predictors of Hyperlactatemia

	Univariate Analysis		Multivariate Analysis	
Risk factor	OR (%95 CI)	P	OR (%95 CI)	P
Age	1,017(,993-1,043)	0,169	1,027(,994-1,060)	0,105
Gender: Famele	,827(,482-1,421)	0,493	1,048(,486-2,262)	0,904
EuoroSCORE II	1,216(1,030-1,435)	,021*	,918(,701-1,203)	0,535
DM	,685(,411-1,142)	0,146	,549(,275-1,098)	0,09
LVEF<45%	,810(,363-1,810)	0,608	1,896(,589-6,097)	0,283
CPB duration	1,018(1,013-1,024)	,000**	1,020(1,004-1,036)	,015*
Aortic cross-clamping duration	1,016(1,010-1,022)	,000**	,995(,979-1,012)	0,596
Nadir hematocrit on CPB (%)	,974(,913-1,038)	0,413	1,005(,927-1,090)	0,897
Preoperative MAP-mean CPB pressure	,991(,975-1,008)	0,304	,998(,977-1,021)	0,891
Mean CPB pressure	,989(,962-1,018)	0,461	,992(,956-1,029)	0,657
Mean CPB flow (L/min)	,927(,543-1,582)	0,782	1,510(,752-3,034)	0,247
Need of inotropic agents on CPB	3,112(1,839-5,265)	,000**	,847(,390-1,840)	0,674
Use of inotropic agents in ICU	4,696(2,818-7,826)	,000**	2,729(1,263-5,897)	,011*
Dialysis	3,650(1,475-9,033)	,005**	1,047(,274-3,994)	0,946
Re-operation	3,181(1,479-6,841)	,003**	,870(,282-2,686)	0,808
IABP	18,167(6,788-48,621)	,000**	8,552(2,470-29,602)	,001**
ECMO	45,397(5,499-74,742)	,000**	29,947(2,578-47,934)	,007**
Ventilation time >24h	10,419(5,275-20,580)	,000**	3,837(1,532-9,610)	,004**

**p<0,01 *p<0,05, DM: Diabetes Mellitus, LVEF: Left ventricular ejection fraction, CPB: Cardiopulmonary bypass, MAP: Mean arterial pressure, IABP: Intra-aortic balloon pump, ECMO: Extracorporeal Membrane Oxygenation

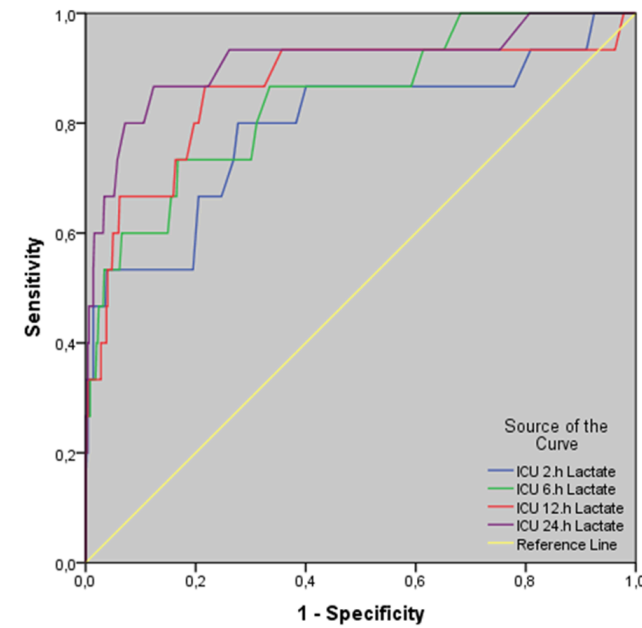| Lactate	AUC	SE	p	95% CI
ICU2h	,793	,074	,000**	,649-,937
ICU6h	,842	,056	,000**	,733-,952
ICU12h	,860	,063	,000**	,737-,984
ICU24h	,911	,051	,000**	,812-1,000

Figure 1. Receiver operating characteristics (ROC) curve for lactate levels as a predictor of mortality.AUC: Area Under the Curve; CI: confidence interval

p <0.01) was found to be 3.05 mmol/L (sensitivity 86.7% and specificity 87.6%).

The patients were divided into two groups according to the lactate value of 3.05mmol/L; Group 1 (Lactate <3.05 mmol/L, n = 442) and Group 2 (Lactate ≥ 3.05 mmol/L, n = 75). Age, gender, BMI, MAP, EF, serum creatinine, preoperative lactate, and comorbidities were similar between the two groups. The EuroSCORE II value was found to be significantly higher in the group with HL (p = 0.018) (Table 1).

There was no significant difference between the two groups in the lowest on-pump hematocrit value, erythrocyte suspension delivered on the pump, the mean CPB pressure, the MAP-mean CPB pressure difference, and the mean CPB flow. Patients with HL had significantly longer CPB time (162.4 ± 54.2 vs. 124.0 ± 38.7 min; p = 0.000) and ACC time (107.1 ± 48.1 vs. 79, 8 ± 35.0 min; p = 0.000) and more on-pump inotropic agent requirements (69.3% versus 42.1%; p = 0.000) (Table 2).

Postoperative complications are shown in Table 2. In the comparison between the two groups, there was no statistical difference in terms of bleeding, infection, and CVD values. There were statistical differences in terms of ventilation time, length of stay in ICU and length of the hospital stay, prolonged ventilation (> 24h), reoperation, dialysis, IABP, ECMO, use of inotropic agents in the intensive care unit, and mortality. In patients in the HL group, the ventilation time was 25.0 ± 26.9 hours, the length of stay in ICU was 5.4 ± 4.3 days, and the length of the hospital stay was 10.9±6.0 days. Prolonged ventilation was found to be 30.7%, re-operation: 14.9%, dialysis: 10.7%, IABP use: 20.0%, ECMO use: 9.3%, and use of inotropic agents in the intensive care unit: 60.0% (p<0.01). While the mortality rate was 0.5% in the group with lactate <3.05 mmol/L, it was 17.3% in the group with lactate ≥3.05 mmol/L (p =. 000).

Table 3 shows logistic regression analysis for HL risk factors. According to the univariate analysis, risk factors were found to be EuroSCORE II, CPB time, and ACC time, on-pump inotropic agent requirement, use of inotropic agents in the intensive care unit, dialysis, reoperation, IABP, ECMO, and prolonged ventilation (> 24h) (p <0.05). In the Multivariate analysis made accordingly, CPB time, use of inotropic agents in the intensive care unit, IABP, ECMO, and prolonged ventilation (> 24h) were found to be independent risk factors for HL (p <0.05).

Discussion

In our study, the lactate level ≥3.05 mmol/L at the postoperative 24th hour in adult patients undergoing open-heart surgery has been shown to be associated with postoperative complications and mortality. Besides, in multivariate analysis, CPB time, use of inotropic agents in the intensive care unit, use of IABP and ECMO, and prolonged ventilation time were identified to be independent risk factors for the development of HL.

In the literature, lactate values between 2-5 mmol/L were considered to be the threshold value for HL identification after open-heart surgery [2, 8,11,12]. Besides, the incidence of HL in patients was reported to be 10-20% [9,11,12]. In our study, we determined the cut-off value for HL as 3.05 mmol/L with ROC analysis, and we found the HL incidence to be 14.5%, which consistent with the literature.

Studies have reported that HL-related conditions are age,

gender, congestive heart failure, low left ventricular ejection fraction, hypertension, diabetes, peripheral circulatory failure, and emergency cases [9-11, 13-18]. When preoperative data that may affect HL in our own patient population were examined, it has been shown that factors such as age, gender, low EF, and comorbidities alone are not effective in the development of hyperlactatemia. In our patient population, it was determined from preoperative data that the EuroSCORE II value was higher in patients with HL. As the EuroSCORE II value is a scoring system consisting of preoperative data, we think that HL is not due to a single cause but multifactorial.

In open-heart surgery, patient management during the CPB time needed in the intraoperative period is vital. Tissue perfusion and circulatory support should be provided effectively throughout the CPB time. Deterioration of cell oxygen delivery during the CPB period and consequently, the activation of the anaerobic metabolic mechanism is the most important reason that increases the lactate level during the perfusion period [5, 6,8,9,11,12].

As stated in Table 2, in our study, during the CPB period, the lowest hematocrit value, mean CPB pressure, MAP-mean CPB pressure difference, and mean CPB flow were similar in both groups and could not be associated with HL. We attribute this to our standardization of parameters such as temperature, flow, perfusion pressure, and avoiding hyperglycemia and hemodilution during the CPB period. While CPB management could be standardized in each patient, the CPB time could not be standardized due to the variable surgical teams and the presence of different cardiac cases, and lactate levels were found to be higher in patients with long CPB time. Lactate levels were found to be higher in patients who needed inotropic support to provide pump perfusion at a certain level in each patient.

HL is known to be bimodal in cardiac surgery [19-21]. Early-onset HL is hyperlactatemia that develops in the operating room or very early following ICU admission. Late-onset HL, on the other hand, is a clinical condition that typically arises within 6-12 hours of ICU admission and continues for up to 24 hours [20]. Hyperlactatemia in our series complies with late-onset HL. While early-onset HL is associated with CPB time, hemodilution, and co-morbidities [11], late-onset HL is associated with the use of β2-agonists such as epinephrine [20], limb ischemia due to the use of mechanical cardiovascular support devices (ECMO and IABP), hepatosplenic and mesenteric ischemia [15]. In our study, the causes of late-onset HL were shown to be patients showing inotropic agent support in the intensive care unit, the use of mechanical support devices (IABP and ECMO), and prolonged mechanical ventilation time. Other causes, which include hepatosplenic and mesenteric ischemia were not present in our patient population [6,9,14,18].

In a cohort study of patients who underwent cardiac surgery and stayed in the intensive care unit for more than 24 hours, the peak lactate level was 3 mmol/L and above, and it was stated that the effect of persistent hyperlactatemia on postoperative morbidity and mortality was higher than that of the highest lactate level at the end of the study [18]. In our study, lactate levels were monitored up to the 24th hour in the ICU. We found that lactate levels that continued to be elevated at the 24th

hour were more specific in predicting postoperative morbidity and mortality.

There are many publications reporting that high blood lactate levels are associated with increased postoperative morbidity and mortality in both adult and pediatric cardiac surgery. The common view is that regular and continuous monitoring of lactate levels in the perioperative period will provide success in clinical treatment, and will also shorten the hospital and intensive care periods and bring a cost-effective treatment [1-4, 6,7,22-24]. In our study, patients in the HL group had significantly longer ventilation time (p = 0.000), and length of stay in ICU (p = 0.000) and the length of the hospital stay (p = 0.000). The mortality rate was found to be higher in patients in the HL group (p = 0.000).

Conclusion

According to our study, 3.05 mmol/L lactate threshold value at 24 hours predicts postoperative mortality in adult patients who underwent open-heart surgery. In addition, this value is significantly associated with prolonged ventilation time, prolonged ICU stay, and hospital stay.

Limitations: We consider the variable CPB and PCO times as a result of operations performed by different surgical teams, and no assessment of how long lactate levels remain higher after 24 hours in the intensive care unit as limiting factors for this study.

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